File Copy

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FILE 'REGISTRY' ENTERED AT 17:27:23 ON 19 MAR 2001
L17          147 S FLUOROSTYRYL
L18         6871 S CHLOROBENZENE
L19         7066 S SULFONE
L20            0 S L17 AND L18 AND L19
L21            0 S L17 AND L18
L22            7 S L17 AND L19
L23           33 S CARBOXYSTYRYL
L24         7066 S SULFONE
L25        11643 S CHLOROBENZYL
L26            0 S L23 AND L24 AND L25
L27            1 S L23 AND L24

     FILE 'EMBASE, CAPLUS, BIOSIS, MEDLINE, USPATFULL' ENTERED AT 17:32:50 ON
     19 MAR 2001
L28            0 S 6178-76-3/RN
L29        64924 S SULFONE
L30        18713 S CYTOPROTECT?
L31           94 S L29 AND L30
L32           87 S L31 AND PY<=1999
L33           83 DUP REM L32 (4 DUPLICATES REMOVED)
L34            0 S L33 AND TOPOISOMERASE
L35            5 S L33 AND MITOSIS
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L35 ANSWER 1 OF 5 USPATFULL
AN 95:71366 USPATFULL
TI Polycyclic quinoline, naphthyridine and pyrazinopyridine derivatives
IN Ganguly, Ashit K., Montclair, NJ, United States
Friary, Richard J., West Orange, NJ, United States
Schwerdt, John H., Lake Hiawatha, NJ, United States
Siegel, Marvin I., Woodbridge, NJ, United States
Smith, Sidney R., Ridgewood, NJ, United States
Sybertz, Edmund J., South Orange, NJ, United States
PA Schering Corporation, Kenilworth, NJ, United States (U.S. corporation)
PI US 5439916 19950808 <--
AI US 1990-576319 19900831 (7)
RLI Division of Ser. No. US 1989-307646, filed on 7 Feb 1989, now patented, Pat. No. US 4988705 which is a division of Ser. No. US 1987-17027, filed on 17 Feb 1987, now patented, Pat. No. US 4810708 which is a continuation-in-part of Ser. No. US 1986-861788, filed on 15 May 1986, now abandoned which is a continuation-in-part of Ser. No. US 1985-744865, filed on 13 Jun 1985, now abandoned
DT Utility
LN.CNT 2023
INCL INCLM: 514/293.000
INCLS: 514/242.000; 514/253.000; 514/254.000; 514/269.000; 514/272.000; 514/273.000; 514/274.000; 514/285.000; 514/287.000; 514/292.000; 546/081.000; 546/082.000; 546/083.000; 546/084.000; 546/064.000; 546/070.000; 544/182.000; 544/238.000; 544/246.000; 544/247.000; 544/249.000; 544/250.000; 544/405.000
NCL NCLM: 514/293.000
NCLS: 514/242.000; 514/252.040; 514/255.050; 514/269.000; 514/272.000; 514/273.000; 514/274.000; 514/285.000; 514/287.000; 514/292.000; 544/182.000; 544/238.000; 544/246.000; 544/247.000; 544/249.000; 544/250.000; 544/405.000; 546/064.000; 546/070.000; 546/081.000; 546/082.000; 546/083.000; 546/084.000
IC [6]
ICM: A61K031-38
ICS: A61K031-395; C07D471-04; C07D239-04
EXF 546/81; 546/82; 546/83; 546/84; 546/64; 546/70; 514/285; 514/287; 514/292; 514/293; 514/242; 514/253; 514/254; 514/269; 514/272; 514/273; 514/274; 544/182; 544/238; 544/246; 544/247; 544/249; 544/250; 544/405
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d kwic

L35 ANSWER 1 OF 5 USPATFULL
PI US 5439916 19950808 <--
DETD . . . caused by such agents. The anti-ulcer activity of the compounds of this invention is identified by tests which measure their **cytoprotective** effect in rats.
DETD The compounds-of this invention may be evaluated for their antiulcer activity characteristics by the procedures which measure the **cytoprotective** effect in rats e.g., as described in Chiu et al., Archives Internationales de Pharmacodynamie et de Therapie, 270, 128-140 (1984).. . .
DETD . . . the condition has improved. Topical applications may then be continued at less frequent intervals (e.g. once a day) to control **mitosis** in order to prevent return of severe disease conditions.

DETD . . . basically the same reaction but employing two equivalents of the peracid oxidant at 25.degree. C. for 50 hrs., the corresponding **sulfone**, 6,7,8,9-tetrahydro-9-(3-methylsulfonylphenyl)-5H-cyclopenta[b][1,8]naphthyridin-5-one is prepared, m.p 271.degree.-273.degree., after crystallization from CH.sub.3 CN. Similarly, starting with 10-(3-chlorophenyl)-6,8,9,10-tetrahydro-5H-thiopyrano[4,3-b][1,8]naphthyridin-5-one or 4-(3-chlorophenyl)-2,3,4,9-tetrahydrothieno [3,2-b][1,8]naphthyridin-9-one and one equivalent. . .

=> d 2-5 kwic bib

L35 ANSWER 2 OF 5 USPATFULL
PI US 5126352 19920630 <--
SUMM . . . caused by such agents. The anti-ulcer activity of the compounds of this invention is identified by tests which measure their **cytoprotective** effect in rats.
SUMM The compounds of this invention may be evaluated for their antiulcer activity characteristics by the procedures which measure the **cytoprotective** effect in rats e.g., as described in Chiu et al., Archives Internationales de Pharmacodynamie et de Therapie, 270, 128-140 (1984).. . .
SUMM . . . the condition has improved. Topical applications may then be continued at less frequent intervals (e.g. once a day) to control **mitosis** in order to prevent return of severe disease conditions.
DETD . . . basically the same reaction but employing two equivalents of the peracid oxidant at 25.degree. C. for 50 hrs., the corresponding **sulfone**, 6,7,8,9-tetrahydro-9-(3-methylsulfonylphenyl)-5H-cyclopenta[b] [1,8]naphthyridin-5-one is prepared, m.p. 271.degree.-273.degree., after crystallization from CH.sub.3 CN. Similarly, starting with 10-(3-chlorophenyl)-6,8,9,10-tetrahydro-5H-thiopyrano[4,3-b] [1,8]naphthyridin-5-one or 4-(3-chlorophenyl)-2,3,4,9-tetrahydrothieno[3,2-b] [1,8]naphthyridin-9-one and. . .
AN 92:53302 USPATFULL
TI Polycyclic quinoline, naphthyridine and pyrazinopyridine derivatives
IN Ganguly, Ashit K., Upper Montclair, NJ, United States
Friary, Richard J., West Orange, NJ, United States
Schwerdt, John H., Lake Hiawatha, NJ, United States
Siegel, Marvin I., Woodbridge, NJ, United States
Smith, Sidney R., Ridgewood, NJ, United States
Seidl, Vera A., Wayne, NJ, United States
Sybertz, Edmund J., South Orange, NJ, United States
PA Schering Corporation, Kenilworth, NJ, United States (U.S. corporation)
PI US 5126352 19920630 <--
AI US 1990-576318 19900831 (7)
RLI Division of Ser. No. US 1989-307646, filed on 7 Feb 1989, now patented, Pat. No. US 4988705 which is a division of Ser. No. US 1987-17027, filed on 17 Feb 1987, now patented, Pat. No. US 4810708 which is a continuation-in-part of Ser. No. US 1986-861788, filed on 15 May 1986, now abandoned which is a continuation-in-part of Ser. No. US 1985-744865, filed on 13 Jun 1985, now abandoned
DT Utility
EXNAM Primary Examiner: Richter, Johann
LREP Nelson, James R.; Blasdale, John H. C.
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2013
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L35 ANSWER 3 OF 5 USPATFULL
PI US 5116840 19920526 <--
SUMM . . . caused by such agents. The anti-ulcer activity of the compounds
of this invention is identified by tests which measure their **cytoprotective** effect in rats.
SUMM The compounds of this invention may be evaluated for their antiulcer activity characteristics by the procedures which measure the **cytoprotective** effect in rats e.g., as described in Chiu et al., Archives Internationales de Pharmacodynamie et de Therapie, 270, 128-140
(1984).. . .
SUMM . . . the condition has improved. Topical applications may then be continued at less frequent intervals (e.g. once a day) to control **mitosis** in order to prevent return of severe disease conditions.
DETD . . . basically the same reaction but employing two equivalents of the peracid oxidant at 25.degree. C. for 50 hrs., the corresponding **sulfone**, 6,7,8,9-tetrahydro-9-(3-methylsulfonylphenyl)-5H-cyclopenta[b][1,8]naphthyridin-5-one is prepared, m.p. 271.degree.-273.degree., after crystallization from CH.sub.3 CN. Similarly, starting with 10-(3-chlorophenyl)-6,8,9,10-tetrahydro-5H-thiopyrano[4,3-b][1,8]naphthyridin-5-one or 4-(3-chlorophenyl)-2,3,4,9-tetrahydrothieno[3,2-b][1,8]naphthyridin-9-one and one equivalent of.
.
.
AN 92:42766 USPATFULL
TI Polycyclic quinoline, naphthyridine and pyrazinopyridine derivatives
IN Ganguly, Ashit K., Upper Montclair, NJ, United States
Friary, Richard J., West Orange, NJ, United States
Schwerdt, John H., Lake Hiawatha, NJ, United States
Siegel, Marvin I., Woodbridge, NJ, United States
Smith, Sidney R., Ridgewood, NJ, United States
Seidl, Vera A., Wayne, NJ, United States
Sybertz, Edmund J., South Orange, NJ, United States
PA Schering Corporation, Kenilworth, NJ, United States (U.S. corporation)
PI US 5116840 19920526 <--
AI US 1990-576640 19900831 (7)
RLI Division of Ser. No. US 1989-307646, filed on 7 Feb 1989, now patented, Pat. No. US 4988705 which is a division of Ser. No. US 1987-17027, filed
on 17 Feb 1987, now patented, Pat. No. US 4810708 which is a continuation-in-part of Ser. No. US 1986-861788, filed on 15 May 1986, now abandoned which is a continuation-in-part of Ser. No. US 1985-744865, filed on 13 Jun 1985, now abandoned
DT Utility
EXNAM Primary Examiner: Rotman, Alan L.
LREP Nelson, James R.; Blasdale, John H. C.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1898
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L35 ANSWER 4 OF 5 USPATFULL
PI US 4988705 19910129 <--
DETD . . . caused by such agents. The anti-ulcer activity of the compounds
of this invention is identified by tests which measure their **cytoprotective** effect in rats.
DETD The compounds of this invention may be evaluated for their antiulcer activity characteristics by the procedures which measure the **cytoprotective** effect in rats e.g., as described in Chiu et al., Archives Internationales de Pharmacodynamie et de Therapie, 270, 128-140
(1984).. . .
DETD . . . the condition has improved. Topical applications may then be

continued at less frequent intervals (e.g. once a day) to control **mitosis** in order to prevent return of severe disease conditions.

DETD . . . basically the same reaction but employing two equivalents of the peracid oxidant at 25.degree. C. for 50 hrs., the corresponding **sulfone**, 6,7,8,9-tetrahydro-9-(3-methylsulfonylphenyl)-5H-cyclopenta[b][1,8]naphthyridin-5-one is prepared, m.p. 271.degree.-273.degree. , after crystallization from CH.sub.3 CN. Similarly, starting with 10-(3-chlorophenyl)-6,8,9,10-tetrahydro-5H-thiopyrano[4,3-b][1,8]naphthyridin-5-one or 4-(3-chlorophenyl)-2,3,4,9-tetrahydrothieno[3,2-b][1,8]naphthyridin-9-one and one equivalent. .

.

AN 91:8803 USPATFULL

TI Polycyclic quinoline, naphthyridine and pyrazinopyridine derivatives

IN Ganguly, Ashit K., Upper Montclair, NJ, United States
Friary, Richard J., West Orange, NJ, United States
Schwerdt, John H., Lake Hiawatha, NJ, United States
Siegel, Marvin I., Woodbridge, NJ, United States
Smith, Sidney R., Ridgewood, NJ, United States
Seidl, Vera A., Wayne, NJ, United States
Sybertz, Edmund J., South Orange, NJ, United States

PA Schering Corporation, Kenilworth, NJ, United States (U.S. corporation)

PI US 4988705 19910129 <--

AI US 1989-307646 19890207 (7)

RLI Division of Ser. No. US 1987-17027, filed on 17 Feb 1987, now patented, Pat. No. US 4810708 which is a continuation-in-part of Ser. No. US 1986-861788, filed on 15 May 1986, now abandoned which is a continuation-in-part of Ser. No. US 1985-744865, filed on 13 Jun 1985, now abandoned

DT Utility

EXNAM Primary Examiner: Lee, Mary C.; Assistant Examiner: Richter, J.

LREP Nelson, James R.; Miller, Stephen I.; Rosen, Gerald S.

CLMN Number of Claims: 19

ECL Exemplary Claim: 1,17

DRWN No Drawings

LN.CNT 2077

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L35 ANSWER 5 OF 5 USPATFULL

PI US 4810708 19890307 <--

SUMM . . . caused by such agents. The anti-ulcer activity of the compounds of this invention is identified by tests which measure their **cytoprotective** effect in rats.

SUMM The compounds of this invention may be evaluated for their antiulcer activity characteristics by the procedures which measure the **cytoprotective** effect in rats e.g., as described in Chiu et al., Archives Internationales de Pharmacodynamie et de Therapie, 270, 128-140 (1984).. . .

SUMM . . . the condition has improved. Topical applications may then be continued at less frequent intervals (e.g. once a day) to control **mitosis** in order to prevent return of severe disease conditions.

DETD . . . basically the same reaction but employing two equivalents of the peracid oxidant at 25.degree. C. for 50 hrs., the corresponding **sulfone**, 6,7,8,9-tetrahydro-9-(3-methylsulfonylphenyl)-5H-cyclopenta[b][1,8]naphthyridin-5one is prepared, m.p. 271.degree.-273.degree., after crystallization from CH.sub.3 CN. Similarly, starting with 10-(3-chlorophenyl)-6,8,9,10-tetrahydro-5H-thiopyrano[4,3-b][1,8]naphthyridin-5-one or 4-(3-chlorophenyl)-2,3,4,9-tetrahydrothieno[3,2-b][1,8]naphthyridin-9-one and one equivalent of.

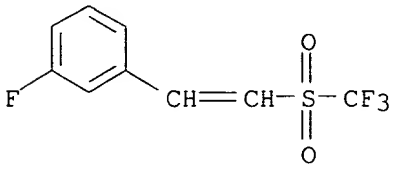
.

.

CLM What is claimed is:
28. A method for treating peptic ulcers in a mammal which comprises administering a **cytoprotective** effective amount of a compound of formula I as defined in claim 1 to said mammal.

AN 89:17309 USPATFULL|
TI Polycyclic quinoline, naphthyridine and pyrazinopyridine derivatives|
IN Ganguly, Ashit K., Upper Montclair, NJ, United States
Friary, Richard J., West Orange, NJ, United States
Schwerdt, John H., Lake Hiawatha, NJ, United States
Siegel, Marvin I., Woodbridge, NJ, United States
Smith, Sidney R., Ridgewood, NJ, United States
Seidl, Vera A., Wayne, NJ, United States
Sybertz, Edmund J., South Orange, NJ, United States
PA Schering Corporation, Kenilworth, NJ, United States (U.S. corporation)
PI US 4810708 19890307 <--
AI US 1987-17027 19870217 (7)
RLI Continuation-in-part of Ser. No. US 1986-861788, filed on 15 May 1986, now abandoned which is a continuation-in-part of Ser. No. US 1985-744865, filed on 13 Jun 1985, now abandoned
DT Utility|
EXNAM Primary Examiner: Lee, Mary C.; Assistant Examiner: Richter, J.|
LREP Billups, Richard C.; Nelson, James R.; Miller, Stephen I.|
CLMN Number of Claims: 36|
ECL Exemplary Claim: 1,23|
DRWN No Drawings
LN.CNT 2195|
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2001 ACS
RN 6178-76-3 REGISTRY
CN Benzene, 1-fluoro-3-[2-[(trifluoromethyl)sulfonyl]ethenyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Sulfone, m-fluorostyryl trifluoromethyl (7CI)**
FS 3D CONCORD
MF C9 H6 F4 O2 S
LC STN Files: BEILSTEIN*, CAOLD, CHEMCATS
(*File contains numerically searchable property data)



L43 ANSWER 4 OF 9 USPATFULL
PI US 5225421 19930706 <--
AB Compounds having the formula: ##STR1## are **inhibitors** of leukotriene biosynthesis. These compounds are useful as anti asthmatic, anti allergic, anti-inflammatory, and **cytoprotective** agents. They are also useful in treating diarrhea, hypertension, angina, platelet aggregation, cerebral spasm, premature labor, spontaneous abortion, dysmenorrhea, and. . .
SUMM Walton et al., J. Med. Chem., 11, 1252 (1968) teach certain indole 3 acetic acid derivatives assayed for tumor **chemotherapy** activity. Walton et al. teach compounds with an alkanoic acid in the 3-position, rather than in the 2-position, and they. . .
SUMM The present invention relates to compounds having activity as leukotriene biosynthesis **inhibitors**, to methods for their preparation, and to methods and pharmaceutical formulations for using these compounds in mammals (especially humans).
SUMM Because of their activity as leukotriene biosynthesis **inhibitors**, the compounds of the present invention are useful as anti-asthmatic, anti-allergic, and anti-inflammatory agents and are useful in treating allergic. . . in the treatment of inflammatory and allergic diseases of the eye, including allergic conjunctivitis. The compounds are also useful as **cytoprotective** agents and for the treatment of migraine headache.
SUMM The compounds of this invention are **inhibitors** of the biosynthesis of 5-lipoxygenase metabolites of arachidonic acid, such as 5-HPETE, 5-HETE and the leukotrienes. Leukotrienes B.sub.4, C.sub.4, D.sub.4. . .
DETD . . . and the like, and 6) cardiovascular conditions such as angina, endotoxin shock, and the like, and that the compounds are **cytoprotective** agents.
DETD The **cytoprotective** activity of a compound may be observed in both animals and man by noting the increased resistance of the gastrointestinal. . . indomethacin. In addition to lessening the effect of non-steroidal anti inflammatory drugs on the gastrointestinal tract, animal studies show that **cytoprotective** compounds will prevent gastric lesions induced by oral administration of strong acids, strong bases, ethanol, hypertonic saline solutions and the. . .
DETD Two assays can be used to measure **cytoprotective** ability. These assays are; (A) an ethanol-induced lesion assay and (B) an indomethacin-induced ulcer assay and are described in EP. . .
DETD Mouse peritoneal macrophages are treated sequentially with arachidonic acid (labelled with tritium); the compound being evaluated as an **inhibitor**, and a stimulator (zymosan). Metabolites derived from arachidonic acid (PGE.sub.2, 6 keto PG-F.sub.1a and leukotriene C.sub.4) are separated from the. . . medium by extraction and chromatography, and then quantitated by determining the amount of radioactivity (cpm) associated with each of them. **Inhibitors** cause a reduction in the amount of radioactivity (cpm) associated with a given metabolite. (This protocol is identical to that. . .
DETD . . . In general, the daily dose range for anti asthmatic, anti allergic or anti inflammatory use and generally, uses other than **cytoprotection**, lie within the range of from about 0.001 mg to about 100 mg per kg body weight of a mammal,. . .
DETD The exact amount of a compound of the Formula I to be used as a **cytoprotective** agent will depend on, inter alia, whether it is being administered to heal damaged cells or to avoid future damage,. . .
DETD The effective daily dosage level for compounds of Formula I inducing **cytoprotection** in mammals, especially humans, will generally

range from about 0.1 mg/kg to about 100 mg/kg, preferably from about 1 mg/kg. . .

DETD . . . mg to about 1 mg) of a compound of Formula I per kg of body weight per day and for **cytoprotective** use from about 0.1 mg to about 100 mg (preferably from about 1 mg to about 100 mg and more. .

.

DETD . . . per kg of body weight per day, preferably from about 0.1 mg to about 10 mg per kg and for **cytoprotective** use from about 0.1 mg to about 100 mg (preferably from about 1 mg to about 100 mg and more.

. .

DETD . . . compounds of Formula I, the pharmaceutical compositions of the present invention can also contain other active ingredients, such as cyclooxygenase **inhibitors**, non-steroidal anti-inflammatory drugs (NSAIDs), peripheral analgesic agents such as zomepirac, diflunisal and the like. The weight ratio of the compound. . .

DETD Pharmaceutical compositions comprising the Formula I compounds may also contain **inhibitors** of the biosynthesis of the leukotrienes such as are disclosed in EP 138,481 (Apr. 24, 1985), EP 115,394 (Aug. 8,. . .

DETD . . . (May 28, 1980), EP 166,591 (Jan. 1, 1986), or in U.S. Pat. No. 4,237,160. They may also contain histidine decarboxylase **inhibitors** such as .alpha.-fluoromethylhistidine, described in U.S. Pat. No. 4,325,961. The compounds of the Formula I may also be advantageously combined. . . those disclosed in U.S. Pat. Nos. 4,283,408; 4,362,736; and 4,394,508. The pharmaceutical compositions may

also contain a K.sup.+ /H.sup.+ ATPase **inhibitor** such as omeprazole, disclosed in U.S. Pat. No. 4,255,431, and the like. Another useful pharmaceutical composition comprises the Formula I. . .

DETD When the second active ingredient in compositions of this invention is a

thromboxane synthetase **inhibitor**, such **inhibitor** can be as described in UK 2,038,821 (e.g., UK 37248 and dazoxiben hydrochloride), U.S. Pat. No. 4,217,357 (e.g., UK 34787),. . .

DETD a) Preparation of Sulfoxides and **Sulfones** ##STR14###

DETD Sulfoxide and **sulfone** derivatives of I can be prepared by using known oxidizing agents such as meta-chloroperbenzoic acid (m-CPBA), hydrogen peroxide, peracetic acid,. . . and the like, on a sulfoxide or sulfide precursor as illustrated in Method C(a). In a similar way, sulfoxide and **sulfone** derivatives of intermediates such as VII can be prepared. Either limiting the amount of

oxidizing agent or monitoring the course. . .

DETD . . . over MgSO.sub.4. Filtration and concentration gave a yellow solid which was recrystallized from a mixture of hexane-toluene to give the **sulfone** of the starting ester, mp 153.degree.-153.5.degree..

CLM What is claimed is:

6. A method of inducing **cytoprotecting** in a mammal comprising administering to a mammal in need of such treatment a **cytoprotective** amount of a compound of claim 1.

AN 93:54735 USPATFULL|

TI 3-hetero-substituted-N-benzyl-indoles and medical methods of use therefor|

IN Gillard, John W., Baie d'Urfe, Canada
Morton, Howard E., Dollard des Ormeaux, Canada
Fortin, Rejean, Montreal-Nord, Canada
Guindon, Yvan, Montreal, Canada

PA Merck Frosst Canada, Inc., Kirkland, Canada (non-U.S. corporation)

PI US 5225421 19930706 <--

AI US 1991-760443 19910916 (7)

RLI Division of Ser. No. US 1987-130771, filed on 9 Dec 1987, now patented, Pat. No. US 5081138 which is a continuation-in-part of Ser. No. US 1986-942900, filed on 17 Dec 1986, now abandoned

DT Utility|
EXNAM Primary Examiner: Springer, David B.|
LREP Lopez, Gabriel; DiPrima, Joseph F.|
CLMN Number of Claims: 8|
ECL Exemplary Claim: 1|
DRWN No Drawings
LN.CNT 1790|
CAS INDE